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STRUCTURE FILE UPDATES: 11 MAR 2008 HIGHEST RN 1007457-12-6
 DICTIONARY FILE UPDATES: 11 MAR 2008 HIGHEST RN 1007457-12-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

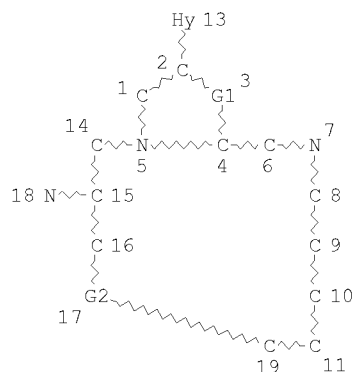
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 L5 STR



REP G1=(0-2) C
 REP G2=(0-4) C
 NODE ATTRIBUTES:
 DEFAULT MLEVEL IS ATOM
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 18

STEREO ATTRIBUTES: NONE
 L7 763 SEA FILE=REGISTRY SSS FUL L5

100.0% PROCESSED 53150 ITERATIONS 763 ANSWERS
 SEARCH TIME: 00.00.02

=> b hcap
 FILE 'HCAPLUS' ENTERED AT 17:31:21 ON 12 MAR 2008
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FILE COVERS 1907 - 12 Mar 2008 VOL 148 ISS 11
FILE LAST UPDATED: 11 Mar 2008 (20080311/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> d bib abs hitrn fhitrn l14 tot

L14 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2008 ACS ON SIN
 AN 2008:192244 HCAPLUS
 TI Preparation of pyridazinonyl macrocyclic peptides as hepatitis C serine
 protease inhibitors
 IN Moore, Joel D.; Tang, Datong; Or, Yat Sun; Wang, Zhe
 PA Enanta Pharmaceuticals, Inc., USA
 SO PCT Int. Appl., 94pp.
 CO DEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------------------|--|----------|------------------|----------|
| PI WO-2008019303 | A2 | 20080214 | 2007MO-US0075146 | 20070803 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, NZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW | | | |
| RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, ME, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AE, BY, KG, KZ, MD, RU, TJ, TM | | | |
| PRAI 2006US-000499844 | A | 20060804 | | |
| GI 2007US-000832893 | A | 20070802 | | |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to macrocyclic compds. I [A = COR1, COR2, COR1R2, SO2NR1, SO2NHR2; R1 = (un)substituted (hetero)aryl, heterocycloalkyl, alk(en)ynyl containing 0-3 heteroatoms selected from O, S or N; cycloalk(en)yl; R2 = H, R1; G = NH5O2R3, R3 = R1 provided that R3 is not CH2Ph or CH2CH2Ph; R4, R5 = independently any of R2; L = CH2; O, S, SO2; X, Y, Z = independently H, CN, NJ, OH and derivs., NH2 and derivs., (un)substituted (hetero)aryl, etc.; or XCCT or XCCT2 = (un)substituted (hetero)aromatic ring; B = (CH2)j; j = 0-4; D = (CH2)k; k = 1-3; U = (CH2)n; n = 0-2; T = (CH2)n; n = 1-3] or their pharmaceutically-acceptable salts, esters or prodrugs which inhibit serine protease activity, particularly the activity of hepatitis C virus (HCV) NS3-NS4A protease. The compds. of the invention interfere with the life cycle of the hepatitis C virus and are also useful as antiviral agents. Thus, macrocycle II was prepared via peptide coupling and ring-closing metathesis reactions. Representative compds. of the invention were found to have HCV activity in the ranges of 0.2 nM - 100 nM in the NS3/NS4A protease enzyme assay and 0.2 nM - 1000 nM in the cell based replicon assay.

IT 1007094-86-1P 1007094-87-2P 1007094-88-3P
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 RL: BYP (Byproduct); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of pyridazinonyl macrocyclic peptides as hepatitis C serine protease inhibitors)

IT 1007094-76-9P 1007094-82-7P
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (preparation of pyridazinonyl macrocyclic peptides as hepatitis C serine protease inhibitors)

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L14 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2008 ACS ON SIN (Continued)

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------------------|--|----------|------------------|----------|
| PI WO-2008019303 | A2 | 20080214 | 2007MO-US0075146 | 20070803 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, NZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW | | | |
| RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, ME, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AE, BY, KG, KZ, MD, RU, TJ, TM | | | |
| PRAI 2006US-000499844 | A | 20060804 | | |
| GI 2007US-000832893 | A | 20070802 | | |

(prepn. of pyridazinonyl macrocyclic peptides as hepatitis C serine protease inhibitors)

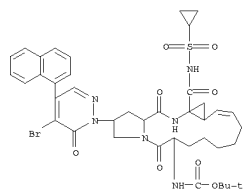
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 (preparation of pyridazinonyl macrocyclic peptides as hepatitis C serine protease inhibitors)

IT 744249-42-1P 744249-43-2P 744249-44-3P
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 1007096-39-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of pyridazinonyl macrocyclic peptides as hepatitis C serine protease inhibitors)

IT 1007094-86-1P
 RL: BYP (Byproduct); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of pyridazinonyl macrocyclic peptides as hepatitis C serine protease inhibitors)

RN 1007094-86-1 HCAPLUS
 CN INDEX NAME NOT YET ASSIGNED

L14 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2008 ACS ON SIN (Continued)



L14 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2008 ACS ON SIN

AN 2008:192063 HCAPLUS
 TI Preparation of tetrazolyl macrocyclic peptides as hepatitis C serine
 protease inhibitors
 IN Sun, Ying; Liu, Dong; Or, Yat Sun; Wang, Zhe
 PA Enanta Pharmaceuticals, Inc., USA
 SO PCT Int. Appl., 100pp.
 CO DEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------------------|--|----------|------------------|----------|
| PI WO-2008019289 | A2 | 20080214 | 2007MO-US0075066 | 20070802 |
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| RW: | AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, ME, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AE, BY, KG, KZ, MD, RU, TJ, TM | | | |
| PRAI 2006US-000499245 | A | 20060804 | | |
| GI 2007US-000832240 | A | 20070802 | | |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

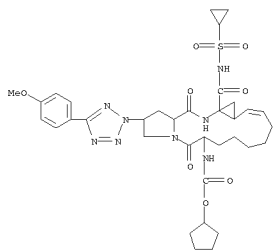
AB The invention relates to macrocyclic compds. I, II, III and IV [A = R1, COR1, COR2, CORNR2, SO2NR1, SO2NHR2; R1 = (un)substituted (hetero)aryl, heterocycloalkyl, alk(en)ynyl containing 0-3 heteroatoms selected from O, S or N, cycloalk(en)yl; R2 = H, R1; G = NH5O2R3, NH5O2NHR4; R3 = R1 provided that R3 is not CH2Ph or CH2CH2Ph; R4, R5 = independently any of R2; L = CH2; O, S, SO2; X = H, R1, NR2; W = absent, O, S, NH, NH2, CORNR5; B = (CH2)j; j = 0-4; D = (CH2)k; k = 1-3; U = (CH2)n; n = 0-2; T = (CH2)n; n = 1-3] or their pharmaceutically-acceptable salts, esters or prodrugs which inhibit serine protease activity, particularly the activity of hepatitis C virus (HCV) NS3-NS4A protease. The compds. of the invention interfere with the life cycle of the hepatitis C virus and are also useful as antiviral agents. Thus, macrocycle V was prepared via peptide coupling and ring-closing metathesis reactions. Representative compds. of the invention were found to have HCV activity in the ranges of 0.2 nM - 100 nM in the NS3/NS4A protease enzyme assay and 0.2 nM - 1000 nM in the cell based replicon assay. Pharmacokinetic anal. of representative compds. showed high liver drug levels. These compds. did not exhibit any significant inhibitions of Cytochrome P 450 enzymes.

IT 1007127-41-4P
 RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of tetrazolyl macrocyclic peptides as hepatitis C serine protease inhibitors)

IT 1007127-18-5P 1007127-19-6P 1007127-20-9P
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L14 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2008 ACS on SIN (Continued)

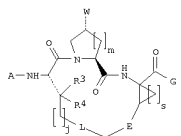
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 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of tetrazolyl macrocyclic peptides as hepatitis C serine protease inhibitors)
 IT 1007128-26-6P 1007128-31-5P
 RL: PRPH (Prophetic); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of tetrazolyl macrocyclic peptides as hepatitis C serine protease inhibitors)
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 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of tetrazolyl macrocyclic peptides as hepatitis C serine protease inhibitors)
 IT 1007127-41-4P
 RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of tetrazolyl macrocyclic peptides as hepatitis C serine protease inhibitors)
 RN 1007127-41-4 HCAPLUS
 CN INDEX NAME NOT YET ASSIGNED



L14 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2008 ACS on SIN

AN 2005:611823 HCAPLUS
 EN 143:153709
 TI Synthesis of macrocyclic hepatitis C virus (HCV) serine protease NS3 inhibitors
 IN Miao, Zhenwei; Sun, Ying; Nakajima, Suanne; Tang, Datong; Wu, Frank; Xu, Guoyou; Or, Yat S.; Wang, Zhe
 PA USA
 SO U.S. Pat. Appl. Publ., 229 pp.
 CODEN: USXCKO
 DT Patent
 LA English
 FAN_CMI 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------------------|------|----------|------------------|----------|
| PI US--2005153877 | A1 | 20050714 | 2004US-000774047 | 20040206 |
| PRAI 2004US-0050969P | P | 20030513 | | |
| OS MAPPAT 143:153709 | | | | |
| GI | | | | |



AB The invention relates to cyclic peptides I [A = H, CO2R, CO2R1, CONHR2, etc.; G = OH, alkoxy, NH502R1, CO2R1, CONHR1, etc.; L = absent, S, SO2, O, COCH2, CFCH2, etc.; j = 0-4; m, s = 0-2; R1, R2 = H, C1-6-alkyl, (substituted)aryl, heteroaryl, etc.; R3, R4 = H, OH, Me, CN, SH, halo, NO2, NH2, amide, MeO, CF3O, CF3; E = CH=CH, CH2CH2; W = (un)substituted heterocyclic ring], or their pharmaceutically-acceptable salts, esters, or prodrugs, which inhibit serine protease activity, particularly the activity of HCV NS3-NS4A protease. An example is I (A = Me3CO2C, G = OH, L = absent, W = 5-phenyl-1,2,3,4-tetrazol-2-yl, j = 3, m, s = 1; R3, R4 = H), which was prepared via peptide coupling and ring-closing metathesis.
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L14 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2008 ACS on SIN (Continued)

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 744250-27-9P 744250-28-OP 744250-29-1P
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 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (synthesis of macrocyclic hepatitis C virus (HCV) serine protease NS3 inhibitors)
 IT 744250-60-OP 744250-61-1P 744250-62-2P
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L14 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2008 ACS on SIN (Continued)

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858951-26-5P 858951-27-6P 858951-28-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis of macrocyclic hepatitis C virus (HCV) serine protease NS3 inhibitors)

IT 858951-29-8P 858951-30-1P 858951-31-2P
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858951-38-9P 858951-39-0P 858951-40-3P
858951-41-4P 858951-42-5P 858951-43-6P

L14 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2008 ACS on SIN (Continued)

858951-44-7P 858951-45-8P 858951-46-9P
858951-47-0P 858951-48-1P 858951-49-2P
858951-50-5P 858951-51-6P 858951-52-7P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis of macrocyclic hepatitis C virus (HCV) serine protease NS3 inhibitors)

IT 744251-08-9P 744251-12-5P 744251-15-8P

744251-18-1P 744251-21-6P 744251-25-0P

744251-32-9P 744251-33-0P 744251-47-6P

744251-51-2P 744251-52-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis of macrocyclic hepatitis C virus (HCV) serine protease NS3 inhibitors)

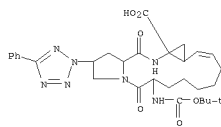
IT 744247-19-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis of macrocyclic hepatitis C virus (HCV) serine protease NS3 inhibitors)

RN 744247-19-6 HCAPLUS

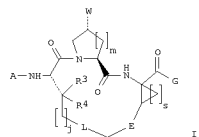
CN Cyclopropa[e]pyrrolol[1,2-a][1,4]diacyclopentadecine-14a(5H)-carboxylic acid, 6-([1,1,1-trimethyl-2-oxo-2-(2-oxo-2-phenyl-1,2,3,6,7,8,9,10,11,13a,14,15,16,16a-tetradecahydro-5,16-dioxo-2-(5-phenyl-2H-tetrazol-2-yl)-], (2R,6S,13aS,14aR,16aS)- (CA INDEX NAME)



L14 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2008 ACS on SIN

AN 2004:698218 HCAPLUS
DN 141:220883
TI Macrocyclic hepatitis C virus (HCV) serine protease NS3 inhibitors, their synthesis and use to prevent HCV infection
IN Miao, Zhenwei; Sun, Ying; Wu, Frank; Nakajima, Suanne; Xu, Guoyou; Or, Yat Sun; Wang, Zhe
PA Enanta Pharmaceuticals, Inc., USA
PX PCT Int. Appl., 299 pp.
CODEN: PXXD2
DT Patent
LA English
FAM.CMI 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|----------|
| PI WO-2004072243 | A2 | 20040826 | 2004WO-US0003479 | 20040206 |
| WO-2004072243 | A1 | 20051103 | | |
| W: AB, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DE, EC, EE, EG, ES, FI, GB, GD, GE, GM, GR, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LZ, LV, MA, MD, MG, MK, MN, MW, MX, MY, NA, NI, NW, BG, GH, GM, KE, LS, LM, ME, SD, SL, SZ, TE, UG, ZM, ZW, AT, BE, BG, CH, CI, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US-2004180915 | A1 | 20040916 | 2003US-000384120 | 20030307 |
| AU-2004211637 | A1 | 20040826 | 2004AU-000211637 | 20040206 |
| CA-2515216 | A1 | 20040826 | 2004CA-00215216 | 20040206 |
| EP-1590442 | A2 | 20051102 | 2004EP-000709020 | 20040206 |
| EP-1590442 | A3 | 20051221 | | |
| R: AT, BE, CH, DE, DK, EE, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| CN-1771050 | A | 20060510 | 2004CN-080009268 | 20040206 |
| JP-2007524576 | T | 20070830 | 2006JP-000503381 | 20040206 |
| PRAI 2003US-000360947 | A | 20030207 | | |
| 2003US-000365854 | A | 20030213 | | |
| 2003US-000384120 | A | 20030307 | | |
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| 2004WO-US0003479 | A | 20040206 | | |
| OS MARPAT 141:220883 | | | | |
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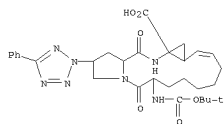


AB The present invention relates to compds. I [A = H, COR2, COOR1, CONHR2, etc.; G = OH, COR2, COOR1, CONHR1, etc.; L = S, SO2, O, COCH2, CF3CH2, etc.; j = 0-4; m, s = 0-2; R1, R2 = H, C1-6-alkyl, (substituted)aryl, heteroaryl, etc.; R3, R4 = H, OH, Me, CN, SH, halo, NO2, NH2, keto, MeO, CF3O, CF3; E = CH=CH, CH2CH2; W = (unsubstituted heterocyclic ring), or a pharmaceutically acceptable salt, ester, or prodrug thereof, and to methods for their synthesis. The compds. inhibit serine protease activity, particularly the activity of HCV NS3-NS4A protease. Consequently, the compds. of the present invention interfere with the life cycle of HCV and are also useful as antiviral agents. The present invention further relates to pharmaceutical compds. comprising the aforementioned compounds, for administration to a subject suffering from HCV infection. The invention also relates to methods of treating an HCV infection in a subject by administering a pharmaceutical composition comprising the compds. of the present invention.

L14 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2008 ACS on SIN (Continued)

IT 744247-19-6P 744247-22-1P 744247-24-3P
744247-36-5P 744247-28-7P 744247-30-1P
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L14 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2008 ACS on SIN (Continued)
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 RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (macrocyclic hepatitis C virus (HCV) serine protease NS3 inhibitors, their synthesis and use to prevent HCV infection)
 IT 744250-60-0P 744250-61-1P 744250-62-2P
 744250-63-3P 744250-64-4P 744250-65-5P
 744250-66-6P 744250-67-7P 745013-11-0P
 746657-33-0P 746657-34-1P 746657-35-2P
 RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (macrocyclic hepatitis C virus (HCV) serine protease NS3 inhibitors, their synthesis and use to prevent HCV infection)
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 744251-18-1P 744251-21-6P 744251-25-0P
 744251-32-9P 744251-33-0P 744251-47-6P
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 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (macrocyclic hepatitis C virus (HCV) serine protease NS3 inhibitors, their synthesis and use to prevent HCV infection)
 IT 744247-19-6P
 RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (macrocyclic hepatitis C virus (HCV) serine protease NS3 inhibitors, their synthesis and use to prevent HCV infection)
 RN 744247-19-6 HCAPLUS
 CN Cyclopropa[e]pyrrolo[1,2-a][1,4]diazacyclopentadecine-14a(5H)-carboxylic acid, 6-[(1,1-dimethylethoxy)carbonyl]amino-1,2,5,6,7,8,9,10,11,13a,14,15,16,16a-tetradecahydro-5,16-dioxo-2-(5-phenyl-2H-tetrazol-2-yl)-, (2R,6S,13aS,14aR,16aS)- (CA INDEX NAME)



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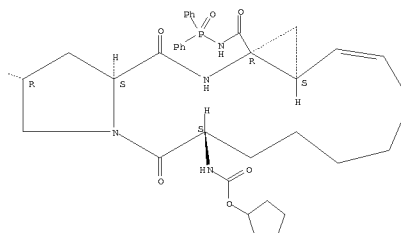
L13 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2008 ACS on SIN
 AN 2008:186295 HCAPLUS
 TI Preparation of phosphorus-containing peptides as hepatitis C serine
 protease inhibitors
 IN Moore, Joel D.; Niu, Deqiang; Xu, Guoyou; Liu, Dong; Or, Yat Sun; Wang,
 Zhe
 PA USA
 SO U.S. Pat. Appl. Publ., 17pp.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------------------|------|----------|------------------|----------|
| US-20080239375 | A1 | 20080214 | 200605-000503407 | 20060811 |
| PRAI 200605-000503407 | | 20060811 | | |

 GI

L13 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2008 ACS on SIN (Continued)

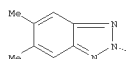
PAGE 1-B



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to phosphorus-containing peptides I and II [A = COOR₁, COR₂, CONHR₂, SO₂R₁, SO₂NHR₂; R₁ = (un)substituted (hetero)aryl, heterocycloalkyl, alk(en)yl, alkynyl containing 0-3 heteroatoms selected from O, S or N, cycloalk(en)yl; R₂ = H, R₁; L = aryl, (un)substituted alk(en)yl, alkynyl containing 0-3 heteroatoms selected from O, S or N, cycloalk(en)yl, heterocycloalkyl; X = absent, O, S, NR₂; T = absent, (un)substituted alk(en)ynylene containing 0-3 heteroatoms selected from O, S or N, (hetero)cycloalkylene; Z = (un)substituted (hetero)aryl; Q = H, SR₁, (un)substituted heterocycloalkyl, cycloalkyl, etc.; W = CH₂, O, S, SO₂, CO, COO, CONH, CHF, CF₂, (un)substituted (hetero)arylene; U, V = independently R₁, XR₂; or UPV = phosphorus-derived heterocyclic moiety; J = (CH₂)_j; j = 0-4; B = (CH₂)_k; k = 1-3; G = (CH₂)_s; s = 0-3; D = (CH₂)_m; m = 0-2; T = (CH₂)_n; n = 1-3] or their pharmaceutically-acceptable salts, esters or prodrugs which inhibit serine protease activity, particularly the activity of hepatitis C virus (HCV) NS3-NS4A protease (no data). The comps. of the invention interfere with the life cycle of the hepatitis C virus and are also useful as antiviral agents. Thus, macrocycle III was prepared via peptide coupling, ring-closing metathesis and reaction with diphenylphosphinamide. Representative comps. of the invention showed biol. activity in enzyme inhibition and cell-based replicon assays for HCV activity (no data).
 IT 1006902-80-2P 1006902-81-3P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of phosphorus-containing peptides as hepatitis C serine protease inhibitors)
 IT 1006902-80-2P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of phosphorus-containing peptides as hepatitis C serine protease inhibitors)
 RN 1006902-80-2 HCAPLUS
 CN INDEX NAME NOT YET ASSIGNED

PAGE 1-A

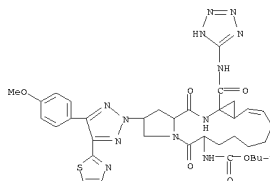


L13 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2008 ACS on SIN
 AN 2008:186295 HCAPLUS
 TI Preparation of acylaminoheteroaryl peptides as hepatitis C serine protease
 inhibitors
 IN Niu, Deqiang; Moore, Joel D.; Liu, Dong; Gai, Yonghua; Chen, Zhiqiang; Or,
 Yat Sun; Wang, Zhe
 PA USA
 SO U.S. Pat. Appl. Publ., 57pp.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| US-2008039470 | A1 | 20080214 | 200605-000503502 | 20060811 |
| WO-2008021956 | A2 | 20080221 | 2007MO-US0075580 | 20070809 |

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 PRAI 200605-000503502 A 20060811
 GI

L13 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2008 ACS on SIN (Continued)



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to peptides I and II [A = H, COOR₁, COR₂, CONHR₂, SO₂R₁, SO₂NHR₂; R₁ = (un)substituted (hetero)aryl, heterocycloalkyl, alk(en)yl, alkynyl containing 0-3 heteroatoms selected from O, S or N, cycloalk(en)yl; R₂ = H, R₁; R₀ = H, Me, Et, OH, CONH₂; U, U₁, U₂ = independently CR₃; R₃ = H, halo, NO₂, CN, aryl, etc.; W, V = independently H, or any of R₂; X = absent, O, S, NR₂; Y = absent, (un)substituted alk(en)ynylene containing 0-3 heteroatoms selected from O, S or N, (hetero)cycloalkylene; Z = (un)substituted (hetero)aryl; L = (CH₂)_j; j = 0-4; Q = (CH₂)_k; k = 1-3; D = (CH₂)_m; m = 0-2; T = (CH₂)_n; n = 1-2] or their pharmaceutically-acceptable salts, esters or prodrugs which inhibit serine protease activity, particularly the activity of hepatitis C virus (HCV) NS3-NS4A protease (no data). The comps. of the invention interfere with the life cycle of the hepatitis C virus and are also useful as antiviral agents. Thus, quinoxaliny macrocycle III was prepared by reaction of alc. IV (preparation given) with 3-(thiophen-2-yl)-1H-quinoxalin-2-one under Mitsunobu conditions, cleavage of the tert-butoxycarbonyl group, treatment with cyclopentyl chloroformate, saponification of the Et ester and coupling of the acid with 5-aminotetrazole. Representative comps. of the invention showed biol. activity in enzyme inhibition and cell-based replicon assays for HCV activity (no data).
 IT 1007204-96-7P 1007205-11-9P 1007205-12-0P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of acylaminoheteroaryl peptides as hepatitis C serine protease inhibitors)
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 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of acylaminoheteroaryl peptides as hepatitis C serine protease inhibitors)
 RN 1007204-96-7 HCAPLUS
 CN INDEX NAME NOT YET ASSIGNED


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CA INDEXING COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPATOLD' ENTERED AT 17:32:07 ON 12 MAR 2008
CA INDEXING COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 17:32:07 ON 12 MAR 2008
CA INDEXING COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

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L16 ANSWER 1 OF 2 USPATFULL on STN
 AN 200517796 USPATFULL
 TI Macrocyclic hepatitis C serine protease inhibitors
 IN Miao, Zhenwei, San Diego, CA, UNITED STATES
 Sun, Ying, Waltham, MA, UNITED STATES
 Nakajima, Suanne, Cambridge, MA, UNITED STATES
 Tang, Datong, Malden, MA, UNITED STATES
 Wu, Frank, Shrewsbury, MA, UNITED STATES
 Xu, Guoyou, Auburndale, MA, UNITED STATES
 Or, Yat S., Watertown, MA, UNITED STATES
 Wang, Zhe, Hockessin, DE, UNITED STATES
 PI US-20050153877 AI 20050714
 AI 2004US-00074047 AI 20040206 (10)
 PRAI 2003US-00050969P 20030213 (60)
 DI Utility
 PG APPLICATION
 LREP EDWARDS & ANGELL, LLP, P.O. BOX 55874, BOSTON, MA, 02205, US
 CLMN Number of Claims: 77
 ECL Exemplary Claim: 1
 DRWN No Drawings
 LN.CNT 7932

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to compounds of Formula I, II or III, or a pharmaceutically acceptable salt, ester, or prodrug, thereof:
 ##STR1## wherein W is a substituted or unsubstituted heterocyclic ring system. The compounds inhibit serine protease activity, particularly the activity of hepatitis C virus (HCV) NS3-NS4A protease. Consequently, the compounds of the present invention interfere with the life cycle of the hepatitis C virus and are also useful as antiviral agents. The present invention further relates to pharmaceutical compositions comprising the aforementioned compounds for administration to a subject suffering from HCV infection. The invention also relates to methods of treating an HCV infection in a subject by administering a pharmaceutical composition comprising the compounds of the present invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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L16 ANSWER 2 OF 2 USPATFULL on STN (Continued)

RN 2004:233741 USPATFULL

TI Pyridazinonyl macrocyclic hepatitis C serine protease inhibitors

IN Nakajima, Suanne, Cambridge, MA, UNITED STATES
Tan, Datong, Malden, MA, UNITED STATES
Wu, Frank, Shrewsbury, MA, UNITED STATES
Miao, Zhenwei, Medway, MA, UNITED STATES
Sun, Ying, Waltham, MA, UNITED STATES
Dr. Yat Sun, Watertown, MA, UNITED STATES
Wang, Zhe, Hockessin, DE, UNITED STATES

PI U5-20040180815 A1 20040916

AI 2003US-000384120 A1 20030307 (10)

DI Utility

FS APPLICATION

LREP ENAMIA PHARMACEUTICALS, INC., ATTN: PATENT DEPT., 500 ARSENAL STREET, WATERTOWN, MA, 02472

CLMN Number of Claims: 16

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 2590

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to compounds of Formula I or II, or a pharmaceutically acceptable salt, ester, or prodrug, thereof: ##STR1##

which inhibit serine protease activity, particularly the activity of hepatitis C virus (HCV) NS3-NS5A protease. Consequently, the compounds of the present invention interfere with the life cycle of the hepatitis C virus and are also useful as antiviral agents. The present invention further relates to pharmaceutical compositions comprising the aforementioned compounds for administration to a subject suffering from HCV infection. The invention also relates to methods of treating an HCV infection in a subject by administering a pharmaceutical composition comprising the compounds of the present invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

II 744247-19-4P 744247-22-1P 744247-24-3P
744247-26-5P 744247-28-7P 744247-30-1P
744247-32-3P 744247-34-5P 744247-36-7P
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(macrocyclic hepatitis C virus (HCV) serine protease NS3 inhibitors, their synthesis and use to prevent HCV infection)

II 744250-59-7P 744250-60-0P 744250-61-1P
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746657-35-2P

(macrocyclic hepatitis C virus (HCV) serine protease NS3 inhibitors, their synthesis and use to prevent HCV infection)

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744251-51-2P 744251-52-3P

(macrocyclic hepatitis C virus (HCV) serine protease NS3 inhibitors, their synthesis and use to prevent HCV infection)

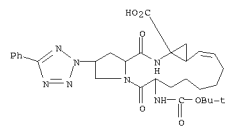
II 744247-19-6P

(macrocyclic hepatitis C virus (HCV) serine protease NS3 inhibitors, their synthesis and use to prevent HCV infection)

RN 744247-19-6 USPATFULL

CN Cyclopropa[e]pyrrolo[1,2-a][1,4]diazacyclotetradecine-14a(5H)-carboxylic acid, 6-((1,1-dimethylethoxy)carbonyl)amino)-1,2,3,6,7,8,9,10,11,13a,14,15,16,16a-tetradecahydro-5,16-dioxo-2-(5-phenyl-2H-tetrazol-2-yl)-, (2R,6S,13aS,14aR,16aS)- (CA INDEX NAME)

L16 ANSWER 2 OF 2 USPATFULL on STN (Continued)



=> d his

(FILE 'HOME' ENTERED AT 17:08:34 ON 12 MAR 2008)

FILE 'HCAPLUS' ENTERED AT 17:08:49 ON 12 MAR 2008
 L1 1 US20050153877/PN

FILE 'REGISTRY' ENTERED AT 17:09:01 ON 12 MAR 2008

FILE 'HCAPLUS' ENTERED AT 17:09:01 ON 12 MAR 2008
 L2 TRA L1 1- RN : 730 TERMS

FILE 'REGISTRY' ENTERED AT 17:09:01 ON 12 MAR 2008

L3 730 SEA L2
 L4 588 L3 AND NRRS>=3
 L5 STR
 L6 40 L5
 L7 763 L5 FULL
 SAV TEM J047C1G1/A L7
 L8 553 L7 AND L3
 L9 210 L7 NOT L8

FILE 'HCAPLUS' ENTERED AT 17:25:28 ON 12 MAR 2008

L10 4 L8
 L11 4 L9
 L12 2 L10 AND L11
 L13 2 L11 NOT L12
 L14 4 L10,L12

FILE 'HCAOLD' ENTERED AT 17:29:44 ON 12 MAR 2008

L15 0 L7

FILE 'USPATFULL, USPATOLD, USPAT2' ENTERED AT 17:29:54 ON 12 MAR 2008

L16 2 L7

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